

University of Groningen

Kinome directed target discovery and validation in unique ovarian clear cell carcinoma models

Caumanns, Joost

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Caumanns, J. (2019). *Kinome directed target discovery and validation in unique ovarian clear cell carcinoma models*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

**Kinome directed target
discovery and validation in
unique ovarian clear cell
carcinoma models**

Joseph Johannes Caumanns

The research in this thesis was supported by a grant from the Dutch Cancer Society (KWF, RUG2012-5477)

Printing of this thesis was supported by:

- UMCG Graduate School of Medical Sciences
- Stichting Werkgroep Interne Oncologie
- University of Groningen

ISBN: 978-94-034-1303-7

Cover: A.M. Heijink, J.J. Caumanns

lay-out design: A.M. Heijink, J.J. Caumanns, & N. van den Tempel

Printing: Ipskamp Printing

Copyright © 2019, J.J. Caumanns

All rights reserved. No part of this thesis may be reproduced, stored or transmitted in any form or by any means without permission of the author.



university of
 groningen

Kinome directed target discovery and validation in unique ovarian clear cell carcinoma models

Proefschrift

ter verkrijging van de graad van doctor aan de
 Rijksuniversiteit Groningen
 op gezag van de
 rector magnificus prof. dr. E. Sterken
 en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

16 januari 2019 om 16:15 uur

door

Joseph Johannes Caumanns

geboren op 16 November 1990
 te Hengelo (O)

Promotores

Prof. dr. S. de Jong
Prof. dr. A.G.J van der Zee

Co-promotor

dr. G.B.A. Wisman

Beoordelingscommissie

Prof. dr. F.C. Amant
Prof. dr. J.J. Schuringa
Prof. dr. F.A.E Kruyt

TABLE OF CONTENTS

Chapter 1	Introduction and thesis outline	7
Chapter 2	<i>ARID1A</i> mutant ovarian clear cell carcinoma: A clear target for synthetic lethal strategies <i>Biochim Biophys Acta, 2018</i>	17
Chapter 3	<i>ARID1A</i> mutation sensitizes most ovarian clear cell carcinomas to BET inhibitors <i>Oncogene, 2018</i>	35
Chapter 4	Integrative kinome profiling identifies mTORC1/2 inhibition as treatment strategy in ovarian clear cell carcinoma <i>Clinical Cancer Research, 2018</i>	61
Chapter 5	Low-dose triple drug combination targeting the PI3K/AKT/mTOR pathway and the MAPK pathway is a highly effective approach in ovarian clear cell carcinoma <i>Submitted</i>	97
Chapter 6	Establishment and characterization of ovarian clear cell carcinoma patient-derived xenograft models <i>Manuscript in preparation</i>	117
Chapter 7	Summary and discussion	137
Appendix	Nederlandse samenvatting List of abbreviations Biography List of publications Dankwoord	150
